ANS

March 8, 2000

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Mr. Lyle D. Jaffe
Dockets Management Branch
Department of Health & Human Services
HFA – 305
Food and Drug Administration
Rockville, MD 20857

Re: 00P- 0788 / CCP 1

Dear Mr. Jaffe,

This letter is in response to your letter informing ANS of the Docket Management Branch's receipt of the Totally Implanted Spinal Cord Stimulator for Pain Relief reclassification petition.

We want to clarify the use of the term "file" in your letter to ANS. ANS submitted the petition on June 11, 1999 and FDA officially received it on June 16, 1999. The reclassification petition was assigned a docket "file" number on 02/29/00.

It is our position that the petition was "filed" on the date that FDA received it. This receipt date was documented in the attached FDA petition review memorandum dated August 6,1999.

We believe that clarifying our interpretation of this term will prevent any future miscommunication.

Sincerely,

Drew Johnson
Director, Regulatory Affairs

cc: Russ Pagano, Ph.D. - FDA
Larry Pilot - McKenna & Cuneo, L.L.P.

30P-0788

ADVANCED NEUROMODULATION SYSTEMS, INC.
6501 WINDCREST DRIVE, SUITE 100 / PLANO, TEXAS 75024 / 972 309-8000 / FAX: 972 309-8150

LET 1

DATE: 8-6-99

FROM: Kristen A. Bowsher, Ph.D., Biomedical and Electrical Engineer
ODE/DGRD/REDB

SUBJECTS: Section 513(f) Reclassification Petition for "Totally Implanted Spinal Cord Stimulators for Pain Relief"

PETITIONER: Advanced Neuromodulation Systems (ANS), Inc.
Plano, Texas
Dated: June 11, 1999
Received: June 16, 1999

REGULATORY CLASSIFICATIONS

Totally implanted spinal cord stimulators for the use as an aid in the management of chronic, intractable pain are class III devices requiring premarket approval (PMA). Implanted spinal cord stimulators for pain relief [21 CFR 882.5880] are class II devices requiring premarket notification (510(k)) clearance.

Approved PMAs for Totally Implanted Spinal Cord Stimulators:
P800040 – Cordis Corporation (approved April 14, 1981)
P840001 – Medtronic, Inc. (approved November 30, 1984)

DEVICE DESCRIPTIONS

The basic components of any spinal cord stimulator are a pulse generator, leads and electrodes. The pulse generator of the implanted spinal cord stimulators consists of a radio-frequency (RF) transmitter and antenna worn externally by the patient and an implanted passive receiver. RF energy is generated by the transmitter and coupled by the antenna through the patients intact skin to the implanted receiver. The totally implanted spinal cord stimulator consists of an implanted pulse generator (IPG) that contains an internal power source that is implanted in the patient.

Independent of the type of pulse generator used, two different lead/electrode systems can be used: percutaneously placed electrode leads or paddle electrodes that require laminectomies to place the electrodes. Percutaneous electrodes are inserted into the epidural space. The lead from the electrodes may then be connected to an external generator, allowing a trial period of stimulation. The lead may then be connected subcutaneously to an implanted RF controlled receiver or to an IPG. Paddle type leads require implantation into the epidural space via laminectomy. The leads are then connected subcutaneously to a radio-controlled receiver or an IPG.

DEVICE DIFFERENCES

The main difference between the two devices is the location of the pulse generator power source. The pulse generator for the totally implanted spinal cord stimulators is implanted into the patient while the pulse generator for the implanted spinal cord stimulators is powered by an external pulse generator that is RF coupled to an implanted receiver.

PETITION OVERVIEW

Advanced Neuromodulation Systems (ANS), Inc. is requesting that the totally implanted spinal cord stimulator for pain relief be reclassified from class III to class II under section 513 (f) of the Food Drug and Cosmetic Act.

Basis for Reclassification Request

The sponsor states that the implanted spinal cord stimulator has been in commercial distribution since 1966. Food and Drug Administration (FDA) classified the device into commercial distribution in 1989. The sponsor believes that the regulatory pathway for these class II (510(k)) implantable spinal cord stimulators is appropriate to control the risks of health associated with of the device.

The sponsor states that the only difference between the class II and class III spinal cord stimulators is that the pulse generator of the class III device is implanted instead of being external. The sponsor claims that the implantation of the generator power source neither affects the intended use of the device nor alters the risk to the health of the patient. The sponsor states that there are no new surgical risks associated with implanting the generator versus implanting a RF receiver.

The sponsor states that at least one class III totally implanted device has been in commercial distribution for over ten years. The sponsor claims that the safety and effectiveness of the totally implanted device as reflected by FDA documents available to the public and in the published literature demonstrate that the controls applicable to class II devices are adequate to provide reasonable assurance of safety and effectiveness.

In summary the sponsor's request for reclassification on the belief that the risks to health associated with the class III totally implanted device are similar to class II implanted stimulators used for the same indication. Therefore, the sponsor believes that the special controls and general controls currently available for the class II spinal cord stimulators will reasonably assure the safety and effectiveness of the class II totally implanted spinal cord stimulators.

Risks Associated with Spinal Cord Stimulation (SCS)

The sponsor listed the reported complications for SCS devices (IPG and RF) in Table 1A and 1B. The sponsor has provided data available from an article by Turner et al. that summarizes the findings of 39 English and French language articles from 1966 to June 1994 and 31 English language articles found via a MEDLINE search. MDR reports for IPG devices were collected from the FDA website which covers the years 1984 through 1996 (data from 1991 was not able to be downloaded). For reports occurring after 1996, a search engine at the FDA MAUDE site was used. These data are summarized in Table 2. Note that definition and reporting of these events are not consistent throughout the literature, and therefore, the summary given by the sponsor in Table 2 should be viewed accordingly.

The most common risk to health associated with both types of SCS is lead migration. Other risks to health include the following: infection, epidural hemorrhage, seroma, hematoma and/or paralysis, CSF leakage, undesirable changes in stimulation, pain at implant sites, allergic or rejection response to implanted materials, local skin erosion over implant, and device failure (lead breakage, hardware malfunction, loose connection). These risks to health are all associated with both the IPG and RF coupled devices.

Additional Risks Associated with IPG

Battery depletion is a risk to health that is associated with the IPG and not the RF coupled device because re-operation is required to replace the battery in an IPG. When a battery requires replacement before the expected date (usually 2 to 3 years post-implantation according to sponsor) it is considered a battery failure. The results of the sponsor's literature search demonstrated that battery failure occurred in 28 of the 1538 cases (1.8%) of the time, although in 22 out of 28 cases the battery failure occurred after more than 3 years (see table 1 B). Note that these 1538 cases include both IPG and RF coupled devices.

The sponsor states that nine studies reported on re-operation due to battery depletion. De La Porte and Van de Kelft, 1993 and Fiume et al., 1995 each reported on eight cases of battery depletion. Meglio et al., 1994 reported on four cases, Francavigilia et al., 1994 reported on two cases that required re-operation due to battery depletion. The sponsor states that the average follow-up period for all these studies was greater than the average expected battery life (approximately three years). The sponsor also cites literature references that report early battery depletion in a patient with very high intensity requirements and three patients who used the stimulator 24 hours a day. Battery failure was reported in 66 MDRs. Complications resulting from re-operation to replace the battery were not reported in the literature.

Proposed Special Controls – (see attached Table 1C)

The special controls available for this risk include consensus standards, such as:

- EN 1441, "Medical Device Risk Analysis";
- EN/IEC 60601 series;
- ANSI/AAMI NS14-1995 "Implantable Spinal Cord Stimulators"; and
- EN 45502-1 "Active Implantable Medical Device - General Requirements for Safety and labeling guidance Medical Device Labeling: Suggested Format and Content".

See the attached Special Control Chart Table 1C.

The sponsor has provided copies of the European Standard for Active Implantable Medical Devices (EN 45502-1) and "Implantable Spinal Cord Stimulator" American National Standard (ANSI/AAMI NS14-1995). Although not the only approach that a class II spinal cord stimulator manufacturer could utilize to obtain marketing clearance the sponsor's proposed special controls are consistent with current FDA review policy of class II spinal cord stimulators.

In addition to using the currently available class II special controls, the petitioner proposes utilizing a chart in the labeling that estimates the life of the battery under specific power consumption conditions be used as the special control.

Comments

The main concern with using an IPG versus a RF coupled system appears to be the increased risk that comes with battery failure. IPG system battery replacement requires additional surgery. The life of a battery in a spinal cord stimulator is affected by various factors including the following:

- battery type;

- output of the stimulator (i.e., voltage, pulse rate, pulse width, frequency);
- number of electrodes used; and
- duration of use.

DRAFT PANEL QUESTIONS

1. Do you believe that there are any other additional risks to health besides those identified in the petition? Please include in your discussion whether the class III totally implanted SCS device is utilized by the same patient population as the class II RF coupled SCS device? If not, are there any risks unique to the class III population?

2. For all of the risks to health identified by the sponsor, are the proposed special controls adequate? If not, are there additional general or special controls that should be utilized? For any additional risks identified in question #1, what general or special controls, if any, might be appropriate to control for the risk(s)?

3. The petitioner requests that the class III totally implantable SCS device should be reclassified into class II from class III. Does the information in the petition and your professional experience support reclassification of the device?

4. The class II SCS device is 510(k) cleared for the aid in the treatment of chronic intractable pain of the trunk and/or limbs. The class III SCS device is a PMA approved device for the same indication. If you believe that the class III SCS device should be reclassified to a class II device, please discuss the appropriate indications for use for the totally implanted SCS device?

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